

28. (New) The method of claim 13, wherein the enzymatic activity of the chimeric enzyme in the unbound state is equivalent to that of the starting enzyme.

*C3*  
*Cont*  
29. (New) The method of claim 13, wherein the enzymatic activity of the chimeric enzyme in the unbound state is equivalent to that of the starting enzyme.

*Pat.*  
IN THE SPECIFICATION:

Please delete the Sequence Listing submitted with the January 21, 2000 Amendment in response to the July 27, 1999 Official Action and insert the revised Sequence Listing, herewith submitted, at the end of the subject specification. At pages 30-35, please delete Tables 1-6 and 8-9 and substitute the revised Tables 1-6 and 8-9. The revised tables include the appropriate "SEQ ID NO" identifier for each sequence listed and the corresponding three letter abbreviation for each amino acid listed in the sequences. No new matter is added. Submitted herewith are two computer readable diskettes, copy 1 and 2, containing the Sequence Listing. The diskettes were encoded using the Microsoft Windows operating system and Microsoft Word as the wordprocessor. All previous computer readable copies are to be deleted.

--Table 1: Sequences and activities of lib 1 A clones selected on 10 µg ampicillin/ml

at 37°C

Clones	Inserted Sequence			Kcat (s <sup>-1</sup> ) <sup>a</sup>
FdBla	Val <sub>103</sub>	- - - Glu <sub>104</sub> Tyr <sub>105</sub>	Ser <sub>106</sub>	ND
Lib1A-01		- - - Val Ser		29
Lib1A-02		- - - Leu His Ser		16
Lib1A-03		Lys Ala Gly Ser Asp Gly (SEQ ID NO: 1)		70
Lib1A-04		Gly Gly Pro Arg Ser Trp (SEQ ID NO: 2)		15
Lib1A-05		Lys Asn Cys Gly Lys Cys (SEQ ID NO: 3)		12
Lib1A-06		Asp Val Pro Gly Ala Gly (SEQ ID NO: 4)		47
Lib1A-07		Lys Ser Gly Glu His Ser (SEQ ID NO: 5)		145
Lib1A-08		- - - Pro Gly Gly		74
Lib1A-09		Arg Ala Gly Asn His Ser (SEQ ID NO: 6)		265
Lib1A-010		Asp Pro Pro Gly Tyr Gly (SEQ ID NO: 7)		9

<sup>a</sup>kcat from phages produced at 23°C (PenG)

ND: not done

Table 2: Sequences and activities of lib1C<sub>4</sub> clones

Clones	Inserted sequence			Kcat (s <sup>-1</sup> ) <sup>a</sup>
FdBla	Val <sub>103</sub>	---- Glu <sub>104</sub> Tyr <sub>105</sub>	Ser <sub>106</sub>	ND
LibC4-11		Arg Phe Gly Asn Asp Trp (SEQ ID NO: 8)		159
LibC4-12		---- Trp Trp		ND
LibC4-13		-- Arg Ser His Trp (SEQ ID NO: 9)		ND
LibC4-14		---- Gln Trp		ND
LibC4-15		Asp Gln Met Gly Gly Gly (SEQ ID NO: 10)		ND
LibC4-16		Arg Ala Gly Ser Thr Trp (SEQ ID NO: 11)		64
LibC4-17		Lys Gly Gly Leu Glu Ser (SEQ ID NO: 12)		721
LibC4-18		---- Ser Asn		ND
LibC4-19		---- Glu Gly		ND

<sup>a</sup>kcats from phages produced at 23°C (PenG)

ND: not done

C<sup>5</sup>  
cont

Table 3: Sequences and activities of lib1D<sub>2</sub> clones

Clones	Inserted sequence			Kcat (s <sup>-1</sup> ) <sup>a</sup>
FdBla	Leu <sub>102</sub>	--- Val <sub>103</sub> Glu <sub>104</sub> Tyr <sub>105</sub>	Ser <sub>106</sub>	ND
Lib1D2-02		--- Val Gly Gly		ND
Lib1D2-03		--- Val Thr Tyr		ND
Lib1D2-04	Phe	--- Gly Thr Trp		ND
Lib1D2-05		Leu Pro Asn Leu Asp Thr (SEQ ID NO: 13)		224
Lib1D2-06		--- Ile Ser Trp		ND
Lib1D2-07		Asn Arg Ser Gly Ser Trp (SEQ ID NO: 14)		2506
Lib1D2-08		Asp Val Ser Gly Gly His (SEQ ID NO: 15)		337
Lib1D2-09		Leu His Ser Gly Gly Trp (SEQ ID NO: 16)		ND
Lib1D2-10		Ser Arg Ala Gly Gly Tyr (SEQ ID NO: 17)		ND

<sup>a</sup>kcats from phages produced at 23°C (PenG)

ND: not done

Table 4: Sequences and activities of several clones from the lib3d library picked from among the 3% most active ones

Clones	Inserted sequence			Kcat (s <sup>-1</sup> ) <sup>a</sup>
FdBla	Ala <sub>270</sub>	- - - Thr <sub>271</sub> Met <sub>272</sub>	Asp <sub>273</sub> Glu <sub>274</sub> Arg <sub>275</sub>	ND
Lib3-01		- - - Ser Met		1133
Lib3-02		- - Ala Thr Thr		203
Lib3-03		Thr Ala Lys Met Asp (SEQ ID NO: 18)		127
Lib3-04	Pro	Pro Thr Val Ser Met (SEQ ID NO: 19)		92
Lib3-05		Arg Gln Ser Thr Met (SEQ ID NO: 20)		48
Lib3-06	Asp	- - Asp Arg Ala		1.1
Lib3-07		Gly Arg Thr Thr Met (SEQ ID NO: 21)		44
Lib3-08		Ser Asp Gln Pro Leu (SEQ ID NO: 22)	Leu	140
Lib3-09		His Thr Ala Ser Met (SEQ ID NO: 23)		137
Lib3-10		- - - Asn Gly		278
Lib3-11		Lys Ser Val Gly Leu (SEQ ID NO: 24)		ND
Lib3-12		Ala Asn Ile Ser Leu (SEQ ID NO: 25)		ND
Lib3-13		- - - Asn Ile		ND
Lib3-14		Pro Val Ala Pro Ile (SEQ ID NO: 26)		ND
Lib3-15		Arg Pro Thr Thr Leu (SEQ ID NO: 27)		ND
Lib3-16		Pro Asn Ala Asn Met (SEQ ID NO: 28)		ND
Lib3-17		- - Ala Thr Thr		ND

<sup>a</sup>kcat from phages produced at 23°C (PenG)

ND: not done

Table 5: Sequences and activities of lib3f clones selected on 10 µg ampicillin/ml at 37°C

Clones	Inserted sequence		Kcat (s <sup>-1</sup> ) <sup>a</sup>
FdBla	Ala <sub>270</sub>	----- Thr <sub>271</sub> Met <sub>272</sub> Asp <sub>273</sub> Glu <sub>274</sub> Arg <sub>275</sub> (SEQ ID NO: 40)	ND
Lib3-18		Ala Thr Ser Phe Ala Pro (SEQ ID NO: 29)	208
Lib3-19		Arg Arg Lys Gln Pro Thr (SEQ ID NO: 30)	32
Lib3-20		Thr Ala His Val Ala Ser (SEQ ID NO: 31)	99
Lib3-21		Thr Asn Lys Gln Pro Ser (SEQ ID NO: 32)	73
Lib3-22		Lys Ser Tyr Thr Pro Glu (SEQ ID NO: 33) Gln	85
Lib3-23		Lys Trp Asn Tyr Thr Thr (SEQ ID NO: 34)	ND
Lib3-24		Gly Glu His Glu Ala Gly (SEQ ID NO: 35)	114
Lib3-25		Glu Glu Asn Gly Arg Pro (SEQ ID NO: 36) Gln	100
Lib3-26		Gln Leu Gln Val Pro Pro (SEQ ID NO: 37)	186
Lib3-27		Ala Pro Gly Asn Asp Gly (SEQ ID NO: 38)	64
Lib3-29		Ala Gly Ala Thr Tyr Glu (SEQ ID NO: 39)	111

<sup>a</sup>kcat from phages produced at 23°C (PenG)

ND: not done

Table 6: Sequences and activities of rec 1 clones selected on 10 µg ampicillin/ml at 37°C

Clones	Leu02	Val03 Glu04 Tyr105	Ser106	Inserted Sequence	Met272	Kcat(s <sup>-1</sup> ) <sup>a</sup>
FdBl				Ala270	Met272	ND
Rec 1-01		Glu Arg Ser Gly His Trp (SEQ ID NO: 41)		---- Thr271 ----- Thr		145
Rec 1-03		--- Val Glu Tyr		Arg Thr Ala Lys Val Ser (SEQ ID NO: 44)		57
Rec 1-04		--- Val Thr Trp		Gln Lys Val Glu Pro Ser (SEQ ID NO: 45)		61
Rec 1-05		--- Val Leu Gly		----- His		145
Rec 1-06		--- Val Gln Gly		Thr Gly Val Tyr Pro Ser (SEQ ID NO: 46)		170
Rec 1-07		--- Cys Met Gly		Gln Gly Pro Trp Ala Ser (SEQ ID NO: 47)		380
Rec 1-09*		--- Ile Glu Gly		Ile Gly Asp Tyr Ser Lys (SEQ ID NO: 48)		251
Rec 1-10		--- Val Asp Trp		Thr Gly Asn Gln Ala Thr (SEQ ID NO: 49)		93
Rec 1-11*		--- Val Ser Gly		Ser Asn Gly Glu His Ser (SEQ ID NO: 50)		54
Rec 1-12		- Leu Ala Ser Gly Tyr (SEQ ID NO: 42)		Ser Gly His Glu Pro Thr (SEQ ID NO: 51)		139
Rec 1-14		--- Val Pro Tyr		Asp Ser Lys Glu Thr Ser (SEQ ID NO: 52)		304
Rec 1-15*		Val Arg Ser Gly Pro Trp (SEQ ID NO: 43)		Thr Ala Arg Trp Ala Asn (SEQ ID NO: 53)		72
Rec 1-16		--- Val Met Gly		Thr Ala Asn Glu His Thr (SEQ ID NO: 54)		155

<sup>a</sup>kcat from phages produced at 23°C (PenG)

ND: not done

\*clones containing an additional mutation (Arg275<sup>1</sup>)

Table 8: Clones selected on psa 10.

Clones	Inserted Sequences	Kcat-psa66(+psa66 (s <sup>-1</sup> ))* S=PenG
FdBla	Val <sub>103</sub> Glu Tyr	Thr <sub>271</sub> Met
P10Aj3	Library <sup>a</sup>	[psa10]=3.3 10 <sup>-7</sup> M 187/179
P10Aj301	Val Glu Tyr	His Pro Gln Asn Asp Asp Met (SEQ ID NO: 59)
P10Aj302	Val Glu Tyr	His Pro Gln Asn Asp Asp Met (SEQ ID NO: 60)
P10Aj303	Val Glu Tyr	His Pro Gln Asn Asp Asp Met (SEQ ID NO: 61)
P10Aj304	Val Glu Tyr	His Pro Gln Gly Asp Asn Met (SEQ ID NO: 62) His Pro Gln Gly Asp Ser Met (SEQ ID NO: 63)
P10Aj305	Val Glu Tyr	His Pro Gln Asn Asp Asp Met (SEQ ID NO: 64)
P10RB3	Library <sup>b</sup>	[psa10]=3.3 10 <sup>-7</sup> M 52/52
P10RB311	Val Arg Tyr	Ser Asp Gly His Arg Leu Met (Arg <sub>275</sub> →Leu) (SEQ ID NO: 65)
P10RB312	Val Lys Ser Gly Val Ala (SEQ ID NO: 55)	Ser Asp Gly His Arg Leu Met (Arg <sub>275</sub> →Leu) (SEQ ID NO: 66)
P10RB313	Val Lys Ser Gly Asn Thr Trp (SEQ ID NO: 56)	Ser Asp Gly His Arg Leu Met (Arg <sub>275</sub> →Leu) (SEQ ID NO: 67)
P10RB314	Val Asp Arg Thr Lys Gly Trp (SEQ ID NO: 57)	Ser Asp Gly His Arg Leu Met (Arg <sub>275</sub> →Leu) (SEQ ID NO: 68)
P10RB315	Val Asp Gly Pro Asn Gly His (SEQ ID NO: 58)	Ser Asp Gly His Arg Leu Met (Arg <sub>275</sub> →Leu) (SEQ ID NO: 69)

<sup>a</sup>lib3j and <sup>b</sup>rec<sup>4b</sup> phages from the third round of selection

\*kcats from phages produced at 23°C



Table 9: Clones selected on psa66.

Clones	Inserted Sequence		Kcat- $\text{psa66}/\text{psa66}(\text{s}^{-1})^*$ ; %age inhibition		
	Val <sub>103</sub> Glu Tyr	Thr <sub>271</sub> Met	S=PenG	S=PADAC	S=Centa
FdBl <sub>a</sub>					
P66Aj3	Library <sup>a</sup>		[ $\text{psa66}$ ]= $3.3 \cdot 10^{-7}\text{M}$	[ $\text{psa66}$ ]= $3.3 \cdot 10^{-7}\text{M}$	
P66Aj306	Val Glu Tyr	Thr Pro Gly Ser Leu Gln Met (Arg <sub>275</sub> → Leu) (SEQ ID NO: 71)	ND	ND	
P66Aj307	Val Glu Tyr	Ser Ala His Gln Asp Tyr Ile (Arg <sub>275</sub> → Leu) (SEQ ID NO: 72)	ND	42.4/42.4; 00%	
P66Aj308	Val Glu Tyr	Thr Pro Gly Ser Leu Gln Met (Arg <sub>275</sub> → Leu) (SEQ ID NO: 73)	ND	ND	
P66Aj309	Val Glu Tyr	Thr Pro Gly Ser Leu Gln Met (Arg <sub>275</sub> → Leu) (SEQ ID NO: 74)	ND	ND	
P66Aj310	Val Glu Tyr	Thr Pro Gly Ser Leu Gln Met (Arg <sub>275</sub> → Leu) (SEQ ID NO: 75)	ND	ND	
P66RB3	Library <sup>b</sup>		[ $\text{psa66}$ ]= $3.3 \cdot 10^{-7}\text{M}$	[ $\text{psa66}$ ]= $3.3 \cdot 10^{-7}\text{M}$	[ $\text{psa66}$ ]= $1.7 \cdot 10^{-6}\text{M}$
P66RB316	Val Lys Gly	Asp Gly Ser Arg Ile Gln Met (Arg <sub>275</sub> → Leu) (SEQ ID NO: 76)	405/326; 20%	23.8/14.2; 41%	12.2/6.7; 45%
P66RB317	Val Lys Gly Gly His Gly Ala (SEQ ID NO: 70)	Thr Leu	182/134; 26%	25.1/13.6; 46%	14.7/7.2; 51%
			ND	28.2/26.5; 06%	ND
				ND	ND

P66RB318	Val Val Gly	Asp Gly Ser Arg Ile Gln Met (Arg <sup>275</sup> → Leu) (SEQ ID NO: 77)	ND	28.6/11.9; 58%	ND	13.8/5.8; 58%	13.3/3.5; 74%
P66RB319	Val Gln Gly	Asp Gly Ser Arg Ile Gln Met (Arg <sup>275</sup> → Leu) (SEQ ID NO: 78)	ND	47.4/32.6; 31%	ND	ND	ND
P66RB321	ND	ND	ND	17.2/09.3; 46%	ND	ND	ND
P66RB322	ND	ND	ND	27.2/23.8; 13%	ND	ND	ND
P66RB323	ND	ND	ND	19.0/13.2; 31%	ND	ND	ND
P66RB324	ND	ND	ND	22.4/15.2; 32%	ND	ND	ND
P66RB325	ND	ND	ND	21.6/14.9; 31%	ND	ND	ND
P66RB326	ND	ND	ND	19.6/19.2; 02%	ND	ND	ND
P66RB327	ND	ND	ND	20.5/19.6; 04%	ND	ND	ND
P66RB328	ND	ND	ND	29.2/15.8; 46%	ND	ND	ND
P66RB329	ND	ND	ND	26.3/14.3; 46%	ND	ND	ND
P66RB330	ND	ND	6015/4273; 29%	647/444; 31%	ND	33.2/46.2; -32%	33.2/53.7; -62%
P66RB331	ND	ND	ND	25.7/14.1; 45%	ND	ND	ND
P66RB332	ND	ND	ND	25.2/23.5; 09%	ND	ND	ND

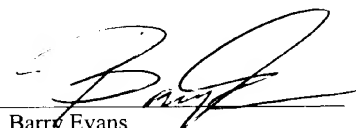
<sup>a</sup>lib3j and <sup>b</sup>rec4b phages from third round of selection

\*kcats from phages produced at 23°C--.

Respectfully submitted,

KRAMER LEVIN NAFTALIS & FRANKEL LLP  
Attorneys for Applicants  
919 Third Avenue  
New York, New York 10022

By: \_\_\_\_\_



Barry Evans

Reg. No. 22,802

Phone: (212) 715-9100

Fax: (212) 715-8000